Bioprosthetic heart valves are made with porcine aortic valves or constructed with bovine pericardium, both cross-linked with glutaraldehyde (GA). The main problem with bioprosthetic valves is tissue degeneration owing to tissue fatigue and calcification [1].

The GA fixation is commonly used to provide resistance to bio-degradability and to reduce the antigenic host response. Unfortunately, the major cause of GA-fixed valve failure is dystrophic calcification. This degeneration occurs due to the aldehyde groups’ phospholipids and immunological response [2].

Particularly, GA fixation does not guarantee complete tissue biocompatibility because it leaves Galactose-alpha-1,3-galactose (aGal) epitopes untouched [2]. Furthermore, implantation of bioprosthetic valves significantly increases the circulating anti-aGal immunoglobulin M and immunoglobulin G already after 10 days of the implantation and these increases seem to persist over time [2–4]. The inactivation of such an epitope should be mandatory to meet the requirements for safe clinical application [2].

Lim et al. propose the development of a new GA-fixed porcine aortic valve treated in five steps, where they combine multiple anticalcification strategies to potentially solve xenograft biocompatibility [5]. The complete decellularization combined with the alpha-galactosidase treatment completely inactivates aGal epitopes and makes the resulting xenograft a great candidate to reduce or even eliminate the antigenic host response. In addition, they extracted phospholipids with an ethanol/octanol solution to reduce the calcification potential of the aldehyde groups. Furthermore, they proved the feasibility of the procedure by first using a mock circulation and then implanting the treated valves in sheep.

The only concern is the sheep model, because it is questionable if an animal that carries the aGal gene is capable of producing a high anti-aGal titre. In our opinion, however, it would be necessary to evaluate the implantation of these new xenografts in a species that already express anti-aGal such as Old World primates.

Currently, no xenograft treatment is able to completely mask or inactivate aGal epitopes. Only valves derived from aGal knockout pigs have been studied with interesting results [6], but this new procedure could be very useful to produce new long-lasting heart valves, maybe even usable in younger patients.

Finally, an intriguing challenge will be to identify biomarkers able to follow and predict valve durability, as well as to identify very early signs of valve failure. Now, we know that biomarkers, depending on their capacity to change over time, can be easily classified into: (i) static markers, which do not change over time and are almost synonymous with genetic markers and (ii) dynamic markers, which change over time. Both static and dynamic markers can be useful in the identification of valve degeneration. Dynamic biomarkers could monitor the status of the valves with a simple blood test performed periodically, whereas static markers could be used to identify patients susceptible to fast prosthetic degradation. In the near future, we expect to see interesting results coming from the collaboration of researchers and clinicians in this very important translational approach to bioprosthetic valve degeneration.

REFERENCES